Inc. The present Amendment and Request for Reconsideration is based upon the substance of the interview.

Applicants have corrected the typographical error in claims 54 and 76 as suggested in the Office Action.

I. The Claimed Inventions Are Not Obvious

Claims 44-50 and 53-64 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of WO 97/05903 (hereinafter, the "Watts reference") and U.S. Patent No. 5,994,062 (hereinafter, the "Mulshine reference). The Office Action asserts that it would have been obvious to combine the composition of the Watts reference with the method of delivery of the Mulshine reference. Applicants traverse the rejection and request reconsideration thereof because the combination of the references fails to produce Applicants' claimed inventions.

The Office Action asserts that the Watts reference teaches a composition comprising a nucleic acid and a mixture of fatty acids. As pointed out during the interview with the Examiner, the Watts reference reports a drug in combination with a mixture "of a fatty acid having 6 to 16 carbon atoms or related mono/diglycerides and a pharmaceutically acceptable dispersing agent" (emphasis added) (see, page 5 of the Watts reference). Subsequent discussions with the Examiner resulted in an agreement that mono/diglycerides of fatty acids were not the same as the fatty acids themselves. Thus, the Watts reference does not teach or suggest the combination of a nucleic acid and at least two fatty acids as recited in claim 44 or the combination of a nucleic acid and capric acid or lauric acid having the modifications recited in claim 61. Thus, the combination of the compositions of the Watts reference with the methods of delivery of the Mulshine reference does not result in the claimed inventions. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

II. The Claims Are Clear And Definite

Claims 25-27, 56, 64, 78 and 80 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being vague and indefinite. Applicants traverse the rejection and respectfully request reconsideration in view of the amended claims.

The Office Action asserts that claim 25 is missing an essential step in that the claim allegedly fails to recite a step for administering the composition to the alimentary canal. As pointed out during the interview, however, claim 25 recites "A method ...comprising **administering**..." (emphasis added). Thus, the step of "administering" is, indeed, recited in claim 25. Thus, claim 25 is definite within the meaning of § 112. *In re Mercier*, 185 U.S.P.Q. 774 (C.C.P.A. 1975) (claims sufficiently define an invention so long as one skilled in the art can determine what subject matter is or is not within the scope of the claims).

The Office Action asserts that the breadth of the ranges of the modifications recited in claims 61 and 64 are considered indefinite. Applicants have amended claims 61 and 64, as recommended during the interview. Thus, the range of modifications recited in claim 64 falls within the scope of the range of modifications recited in claim 61.

Claim 66 has been amended as suggested during the interview to replace the term "oligonucleotide" with the phrase "nucleic acid" to more properly provide antecedent basis.

In addition, claim 80 has been amended, as suggested in the Office Action, to insert the term "further." No change in claim scope has been effected.

In view of the comments and amendments to the claims, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

III. The Claimed Inventions Are Enabled

Claims 25-27, 40 and 66-81 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to enable the full scope of the claimed invention. The Office Action asserts that "claims which recite the use of a nucleic acid must be enabled for all of the stated uses of the nucleic acid" (see, page 7 of the Office Action). The Office Action concludes that Applicants have not

enabled a gene therapy use. Applicants traverse the rejection and request reconsideration thereof because one skilled in the art would be able to practice the claimed inventions without being required to perform undue experimentation.

As a preliminary matter, Applicants are only required to enable the claimed inventions. Indeed, in applying the enablement requirement, the "invention" that must be enabled is that defined by the claims. *Ex parte Erlich*, 3 U.S.P.Q.2d 1011 (Pat. Off. Bd. App. 1987). The Examiner is reminded that claim 25 is directed to methods of "enhancing penetration of an antisense nucleic acid across the alimentary canal of an animal" and that claim 66 is directed to methods of "delivering an antisense nucleic acid to the intestinal mucosa." Applicants' specification amply enables the claimed methods. The Declaration of Dr. Hardee and Dr. Teng showed that the claimed pharmaceutical compositions, in fact, enhance penetration of a nucleic acid across the alimentary canal of an animal. Paragraphs 3-5 of the Declaration describe experiments whereby penetration of an oligonucleotide across the alimentary canal of rats and dogs is enhanced by delivery of the oligonucleotide along with at least two fatty acids. Such examples are also set forth in Applicants' specification in Examples 3, 4 and 13. Indeed, the Office Action acknowledges that the specification "does provide teaching on the introduction of nucleic acids into the blood and generally into the organs of an animal via the enteral pathway" (see, page 4 of the Office Action). Thus, Applicants have amply enabled the claimed inventions. Further, one skilled in the art is not required to perform, and Applicants are not required to enable, gene therapy to practice the claimed inventions. Thus, no amount of undue experimentation is required to practice Applicants' claimed inventions. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

IV. Conclusion

It is respectfully submitted that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested. Attached hereto is a marked-up version of the changes made to the specification and

claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 40, 56, and 78 have been cancelled.

Claim 82 has been added.

Claims 25, 50, 54, 61, 63, 64, 66, 74, 76 and 80 have been amended as follows:

25. (Amended four times) A method of enhancing penetration of [a] an antisense nucleic acid across the alimentary canal of an animal comprising administering to said animal the composition of claim 44, wherein said composition enhances penetration of said nucleic acid across the alimentary canal of said animal.

50. (Amended) The composition of claim 49 wherein said antisense oligonucleotide [modulates] decreases the expression of a cellular adhesion protein or the rate of cellular proliferation.

54. (Amended) The composition of claim 44 wherein said composition is [proylene] propylene glycol based.

61. (Amended twice) A composition comprising a nucleic acid and capric acid or lauric acid or a pharmaceutically acceptable salt thereof, wherein said nucleic acid has at least one chemical modification selected from the group consisting of [a cytosine to 5-methyl-cytosine substitution, a phosphorothioate linkage and a 2'-methoxyethoxy modification] a modified nucleobase and a modified sugar residue.

63. (Amended) The composition of claim 62 wherein said antisense oligonucleotide [modulates] decreases the expression of a cellular adhesion protein or the rate of cellular proliferation.

64. (Amended) The composition of claim 61 wherein said nucleic acid has at least one chemical modification selected from the group consisting of [a modified nucleobase, a modified sugar residue, and a modified backbone linkage] a cytosine to 5-methyl-cytosine substitution and a 2'-methoxyethoxy modification.

66. (Amended) A method of delivering [a] an antisense nucleic acid to the intestinal mucosa comprising contacting the alimentary canal with a composition comprising a nucleic acid and at least two fatty acids, or pharmaceutically acceptable salts thereof, wherein said [oligonucleotide] nucleic acid has at least one chemical modification selected from the group consisting of a cytosine to 5-methyl-cytosine substitution, a phosphorothioate linkage and a 2'-methoxyethoxy modification.

74. (Amended) The method of claim 73 wherein said antisense oligonucleotide [modulates] decreases the expression of a cellular adhesion protein or the rate of cellular proliferation.

76. (Amended) The method of claim 66 wherein said composition is [proylene] propylene glycol based.

80. (Amended) The method of claim 66 wherein said composition further comprises a bile salt.

82. (New claim) A method of delivering an antisense nucleic acid to the intestinal mucosa comprising contacting the alimentary canal with a composition comprising a nucleic acid and capric acid or lauric acid or a pharmaceutically acceptable salt thereof, wherein said nucleic acid has at least one chemical modification selected from the group consisting of a cytosine to 5-methyl-cytosine substitution and a 2'-methoxyethoxy modification.